PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P207556PCT	**FOR FURTHER ACTION**	See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)
International application No. PCT/NL 03/00254	International filing date *(day/month/year)* 04.04.2003	Priority date *(day/month/year)* 04.04.2002
International Patent Classification (IPC) or both national classification and IPC C07K16/28		
Applicant LEIDEN UNIVERSITY MEDICAL CENTER, et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 4 sheets, including this cover sheet.

   ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

   These annexes consist of a total of 2 sheets.

3. This report contains indications relating to the following items:

   - I ☒ Basis of the opinion
   - II ☐ Priority
   - III ☐ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - IV ☐ Lack of unity of invention
   - V ☒ Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - VI ☐ Certain documents cited
   - VII ☐ Certain defects in the international application
   - VIII ☐ Certain observations on the international application

Date of submission of the demand	Date of completion of this report
19.09.2003	22.07.2004
Name and mailing address of the international preliminary examining authority: European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Schwachtgen, J-L Telephone No. +49 89 2399-8933

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/NL 03/00254

I. Basis of the report

1. With regard to the **elements** of the international application *(Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17))*:

Description, Pages

1-29 as originally filed

Claims, Numbers

1-10 received on 24.05.2004 with letter of 24.05.2004

Drawings, Sheets

1/28-28/28 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☒ the claims, Nos.: 10-13
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

   (Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-9
	No:	Claims	
Inventive step (IS)	Yes:	Claims	1-9
	No:	Claims	
Industrial applicability (IA)	Yes:	Claims	1-9
	No:	Claims	

2. Citations and explanations

see separate sheet

Re Item V

Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Reference is made to the following document/s/:
   D1: MELIEF C J M ET AL: 'STRATEGIES FOR IMMUNOTHERAPY OF CANCER' ADVANCES IN IMMUNOLOGY, ACADEMIC PRESS INC., NEW YORK, NY, US, vol. 75, 2000, pages 235-282, XP001027072 ISSN: 0065-2776
   D4: WO 99 61065 A (LEIDEN UNIVERSITY MEDICAL CENT ;TANOX INC (US)) 2 December 1999 (1999-12-02)

2. The document D1 discloses a composition comprising an agonistic anti- CD40 antibody and its use for promoting tumour-specific CD8+ CTL responses (page 252, last 6 lines and references cited therein). D1 further discloses the use of the above composition in combination with the HPV16 class I MHC antigen RAHYNIVTF for the treatment of C3 tumours (page 258, last 6 lines to page 259, lines 1-5; page 259, last 7 lines to page 260, lines 1-2; references cited therein).

3. The document D4 discloses a composition comprising a humanised agonistic anti-CD40 antibody and the use of the said antibody in combination with the HPV16 class I MHC antigen RAHYNIVTF for the manufacture of a medicament to treat tumours (Claims 1-5).

4. The subject-matter of present claims 1-10 differs from the disclosure in D1 and D2, in that the agonistic anti-CD40 antibody is used for the treatment of a tumour or infectious agent, whereby the treatment does not comprise immunisation with an antigen of the tumour or infectious agent. None of the cited prior art documents, either alone or in combination, anticipates the subject-matter of said claims 1-9. Thus, the present application meets the criteria of Article 33(1) PCT, because the subject-matter of claims 1-9 is new and inventive in the sense of Article 33(2) and 33(3) PCT.

New Claims

1. The use of an agonistic anti-CD40 antibody, or a fragment thereof which stimulates the CD40 receptor, in the manufacture of a medicament for the treatment of a tumour or infectious agent by induction of systemic T cell immunity against an antigen of the tumour or infectious agent, whereby the treatment does not comprise immunisation with an antigen of the tumour or infectious agent.

2. The use according to claim 1, wherein the infected or tumour cells do not express the CD40 receptor.

3. The use according to claim 1 or 2 wherein the CD40 receptor targeted by the agonistic anti-CD40 antibody is expressed on the dendritic cells of the treated subject.

4. The use according to any of the preceding claims, wherein the induction of the systemic T cell immunity is a cytotoxic T cell response.

5. The use according to any of the preceding claims, wherein the agonistic anti-CD40 antibody or fragment thereof is human, humanised, chimeric or deimmunised.

6. The use according to any of the preceding claims, wherein the fragment is a V_H, V_L, Fv, Fd, Fab, $(Fab)_2$ or scFv fragment of a human antibody.

7. The use according to any of the preceding claims, wherein the medicament is for injection or oral administration.

8. The use according to any of the preceding claims, wherein the injection is an intra-tumoral injection.

9. The use according to any of the preceding claims, wherein the antigen is a tumour-specific antigen.

10. The use according to any of the preceding claims, wherein the antigen is an antigen of human papilloma virus (HPV) or adenovirus.